CLAIMS

We claim:

1. A method for preparing an injectable microparticle composition for the sustained release of a biologically active agent, comprising the steps of:
   (a) preparing a mixture of a biologically active agent, a biocompatible polymer and a solvent, thereby forming a single phase solvent system;
   (b) removing the solvent from the mixture, thereby forming a polymer/ biologically active agent matrix;
   (c) compressing the matrix using confined pressure compaction at ambient temperature, thereby forming a compressed matrix; and
   (d) fragmenting the compressed matrix, thereby forming the injectable microparticle composition.

2. The method of Claim 1 wherein the biologically active agent is dissolved in the mixture.

3. The method of Claim 1 wherein the biologically active agent is suspended in the mixture.

4. The method of Claim 1 further comprising the step of fragmenting the matrix prior to compressing the matrix.

5. The method of Claim 1 wherein the biocompatible polymer is biodegradable.

6. The method of Claim 1 wherein the biocompatible polymer is selected from the group consisting of poly(lactide)s, poly(glycolide)s, poly(lactide-*co*-glycolide)s, poly(lactic acid)s, poly(glycolic acid)s, polycarbonates, polyesteramides, polyanhydrides, poly(amino acids), polyorthoesters, polyacetals,

polycyanoacrylates, polyetheresters, polycaprolactone, poly(dioxanone)s, poly(alkylene alkylate)s, polyurethanes, and blends and copolymers thereof.

7. The method of Claim 6, wherein the polymer is poly(lactide-*co*-glycolide)-*co*-EMPO.

8. The method of Claim 1 wherein the solvent is removed by evaporation.

9. The method of Claim 1 wherein the solvent is removed by sublimation.

10. The method of Claim 1 wherein the mixture is cast as a film prior to removal of the solvent.

11. The method of Claim 1 wherein the matrix is compressed using a press and die apparatus.

12. The method of Claim 1 wherein the compressed matrix is fragmented by milling.

13. The method of Claim 12 wherein the milling is selected from the group consisting of jet milling, centrifugal milling and hammer milling.

14. The method of Claim 1 wherein the compressed matrix is fragmented under cryogenic conditions.

15. The method of Claim 1 wherein the compressed matrix is fragmented to produce microparticles having a volume median particle size of about 1 to about 1000 microns.

16. The method of Claim 1 wherein the compressed matrix is fragmented to produce microparticles having a volume median particle size of about 500 microns or less.

17. A method for forming an injectable microparticle composition for the sustained release of a biologically active agent, comprising the steps of:

(a) forming a mixture of a biologically active agent, a biocompatible polymer and a polymer solvent;

(b) forming droplets of the mixture;

(c) freezing the droplets, thereby forming frozen droplets;

(d) extracting the polymer solvent from the frozen droplets into a non-solvent, thereby forming a polymer/biologically active agent matrix;

(e) compressing the matrix, thereby forming a compressed matrix; and

(f) fragmenting the compressed matrix, thereby forming the injectable microparticle composition.

18. The method of Claim 17 wherein the biocompatible polymer is biodegradable.

19. The method of Claim 17 wherein the biocompatible polymer is selected from the group consisting of poly(lactide)s, poly(glycolide)s, poly(lactide-*co*-glycolide)s, poly(lactic acid)s, poly(glycolic acid)s, polycarbonates, polyesteramides, polyanhydrides, poly(amino acids), polyorthoesters, polyaetals, polycyanoacrylates, polyetheresters, polycaprolactone, poly(dioxanone)s, poly(alkylene alkylate)s, polyurethanes, and blends and copolymers thereof.

20. The method of Claim 17 wherein the droplets are frozen using a liquefied gas.

21. The method of Claim 17 wherein the droplets are formed by atomizing the mixture.

22. The method of Claim 17 wherein the droplets are microdroplets.

23. The method of Claim 17 wherein the matrix is compressed using confined pressure compaction.

24. The method of Claim 17 wherein the matrix is compressed using a press and die apparatus.

25. The method of Claim 17 wherein the matrix is compressed in the presence of a coolant.

26. The method of Claim17 wherein the compressed matrix is fragmented by milling.

27. The method of Claim 26 wherein the compressed matrix is fragmented by milling selected from the group consisting of jet, centrifugal and hammer milling.

28. The method of Claim 17 wherein the compressed matrix is fragmented in the presence of a coolant.

29. The method of Claim 17 wherein the compressed matrix is fragmented under cryogenic conditions.

30. The method of Claim 17 wherein the compressed matrix is fragmented matrix is fragmented to produce microparticles having a volume median particle size of about 1 micron to about 1000 microns.

31. The method of Claim 17 wherein the compressed matrix is fragmented to produce microparticles having a volume median particle size of about 500 microns or less.

32. The method of Claim 17 wherein the biologically active agent is suspended in the mixture.

33. The method of Claim 17 wherein the biologically active agent is dissolved in the mixture.

34. A method for treating a patient in need of therapy comprising:

administering to the patient a therapeutically effective amount of the injectable microparticle composition made by the method of Claim 17.

35. A method for treating a patient in need of a sustained release of a biologically active agent, comprising:

administering to the patient a therapeutically effective amount of an injectable microparticle composition for sustained release of a biologically active agent prepared by a process including the steps of:

(a) preparing a mixture of a biologically active agent, a biocompatible polymer and a solvent, thereby forming a single phase solvent system;

(b) removing the solvent from the mixture, thereby forming a polymer/ biologically active agent matrix;

(c) compressing the matrix using confined pressure compaction at ambient temperature, thereby forming a compressed matrix; and

(d) fragmenting the compressed matrix, thereby forming the injectable microparticle composition.

36. The method of Claim 35 wherein the biologically active agent is dissolved in the mixture.

37. The method of Claim 35 wherein the biologically active agent is suspended in the mixture.

38. The method of Claim 35 wherein the process for preparing the injectable microparticle composition further comprises the step of fragmenting the polymer/biologically active agent matrix prior to compressing the matrix.

39. The method of Claim 35 wherein the biologically active agent is an antipsychotic drug.

40. The method of Claim 39 wherein the biologically active agent is selected from the group consisting of aripiprazole, olanzapine and risperidone.

41. The method of Claim 39 wherein the patient suffers from an affective disorder.

42. The method of Claim 41 wherein the patient suffers from a condition selected from the group consisting of schizophrenia, depression, and anxiety.

43. Microparticles produced by a process comprising the steps of:

(a) preparing a mixture of a biologically active agent, a biocompatible polymer and a solvent, thereby forming a single phase solvent system;

(b) removing the solvent from the mixture, thereby forming a polymer/ biologically active agent matrix;

(c) compressing the matrix using confined pressure compaction at ambient temperature, thereby forming a compressed matrix; and

(d) fragmenting the compressed matrix, thereby forming the microparticles.

44. The method of Claim 43 wherein the biologically active agent is dissolved in the mixture.

45. The method of Claim 43 wherein the biologically active agent is suspended in the mixture

46. The microparticles of Claim 43 wherein the process for preparing the microparticles further comprises the step of fragmenting the polymer/biologically active agent matrix prior to compressing the matrix.

47. The microparticles of Claim 43 wherein the microparticles have a volume median particle size of about 1 micron to about 1000 microns.

48. The microparticles of Claim 43 wherein the microparticles have a volume median particle size of about 500 microns or less.

49. A pharmaceutical composition comprising the microparticles of Claim 43.

50. Microparticles produced by a process comprising the steps of:

(a) forming a mixture of a biologically active agent, a biocompatible polymer and a polymer solvent;

(b) forming droplets of the mixture;

(c) freezing the droplets, thereby forming frozen droplets;

(d) extracting the polymer solvent from the frozen droplets into a non-solvent, thereby forming a polymer/biologically active agent matrix;

(e) compressing the matrix, thereby forming a compressed matrix; and

(f) fragmenting the compressed matrix, thereby forming the microparticles.

51. The microparticles of Claim 50 wherein the process for preparing the microparticles further comprises the step of fragmenting the polymer/biologically active agent matrix prior to compressing the matrix.

52. The microparticles of Claim 50 wherein the microparticles have a volume median particle size of about 1 micron to about 1000 microns.

53. The microparticles of Claim 50 wherein the microparticles have a volume median particle size of about 500 microns or less.

54. A pharmaceutical composition comprising the microparticles of Claim 50 and a physiologically acceptable vehicle.